5 ANSWER 1 OF 17 BIOSIS COPYRIGHT 2002 BIOLOGICAL ABSTRACTS INC.
ACCESSION NUMBER: 2000:530714 BIOSIS
DOCUMENT NUMBER: PREV200000530714
TITLE: Expression of **heparanase** in normal, dysplastic, and neoplastic human colonic mucosa and stroma: Evidence for its role in colonic tumorigenesis.
AUTHOR(S): Friedmann, Yael; Vlodavsky, Israel (1); Aingorn, Helena; Aviv, Ayelet; Peretz, Tuvia; Pecker, Iris; Pappo, Orit
CORPORATE SOURCE: (1) Department of Oncology, Hadassah Hospital, Jerusalem, 91120 Israel
SOURCE: American Journal of Pathology, (**October, 2000**) Vol. 157, No. 4, pp. 1167-1175. print. ISSN: 0002-9440.
DOCUMENT TYPE: Article
LANGUAGE: English
SUMMARY LANGUAGE: English
AB The human **heparanase** gene, an endo-beta-glucuronidase that cleaves heparan sulfate at specific intrachain sites, has recently been cloned and shown to function in tumor progression and metastatic spread. **Antisense** digoxigenin-labeled **heparanase** RNA probe and monoclonal anti-human **heparanase** antibodies were used to examine the expression of the **heparanase** gene and protein in normal, dysplastic, and neoplastic human colonic mucosa. To our knowledge, this is the first systematic study of **heparanase** expression in human colon cancer. Both the **heparanase** gene and protein were expressed at early stages of neoplasia, already at the stage of adenoma, but were practically not detected in the adjacent normal-looking colon epithelium. Gradually increasing expression of **heparanase** was evident as the cells progressed from severe dysplasia through well-differentiated to poorly differentiated colon carcinoma. Deeply invading colon carcinoma cells showed the highest levels of the **heparanase** mRNA and protein associated with expression of both the gene and enzyme by adjacent desmoplastic stromal fibroblasts. A high expression was also found in colon carcinoma metastases to lung, liver, and lymph nodes, as well as in the accompanying stromal fibroblasts. Moreover, extracts derived from tumor tissue expressed much higher levels of the **heparanase** protein and activity as compared to the normal colon tissue. In all specimens, the **heparanase** gene and protein exhibited the same pattern of expression. These results suggest a role of **heparanase** in colon cancer progression and may have both prognostic and therapeutic applications.

L5 ANSWER 2 OF 17 BIOSIS COPYRIGHT 2002 BIOLOGICAL ABSTRACTS INC.
ACCESSION NUMBER: 1999:367130 BIOSIS
DOCUMENT NUMBER: PREV199900367130
TITLE: All-trans-retinoic acid-mediated growth inhibition involves inhibition of human kinesin-related protein **HsEg5**
AUTHOR(S): Kaiser, Astrid; Brembeck, Felix H.; Nicke, Barbara; Wiedenmann, Bertram; Riecken, Ernst-Otto; Rosewicz, Stefan (1)
CORPORATE SOURCE: (1) Medizinische Klinik m. S. Hepatologie und Gastroenterologie, Charite, Campus Virchow Klinikum, Augustenburgerplatz 1, 13353, Berlin Germany
SOURCE: Journal of Biological Chemistry, (**July 2, 1999**) Vol. 274, No. 27, pp. 18925-18931. ISSN: 0021-9258.
DOCUMENT TYPE: Article
LANGUAGE: English
SUMMARY LANGUAGE: English
AB In this study we used differential display reverse transcription-polymerase chain reaction to search for differentially expressed

all-trans-retinoic acid (ATRA)-responsive genes in pancreatic carcinoma cells. We identified the kinesin-related protein **HsEg5**, which plays an essential role in spindle assembly and spindle function during mitosis, as a novel molecule involved in ATRA-mediated growth inhibition. Using Northern and Western blot analysis we demonstrated that ATRA significantly inhibits **HsEg5** expression in various pancreatic carcinoma cell lines as well as in HaCat keratinocytes. Inhibition of **HsEg5** expression by ATRA occurs at the posttranscriptional level. As a consequence, tumor cells synchronized in S-phase revealed a retarded progression through G2/M phase of the cell cycle indicating that **HsEg5** inhibition results in a delayed progression through mitosis. Furthermore, a significant decrease of **HsEg5** protein expression achieved by **antisense** transfection revealed a significant growth inhibition compared with control cells. Therefore, **HsEg5** represents a novel molecule involved in ATRA-mediated growth inhibition, suggesting that vitamin A derivatives can interact with the bipolar spindle apparatus during mitosis.

L5 ANSWER 3 OF 17 BIOSIS COPYRIGHT 2002 BIOLOGICAL ABSTRACTS INC.
ACCESSION NUMBER: 1998:391490 BIOSIS
DOCUMENT NUMBER: PREV199800391490
TITLE: Expression levels of heat shock factors are not functionally coupled to the rate of expression of heat shock genes.
AUTHOR(S): Victor, Martin; Benecke, Bernd-Joachim (1)
CORPORATE SOURCE: (1) Dep. Biochemistry, Ruhr-Univ. Bochum, 44780 Bochum Germany
SOURCE: Molecular Biology Reports, (**July, 1998**) Vol. 25, No. 3, pp. 135-141.
ISSN: 0301-4851.
DOCUMENT TYPE: Article
LANGUAGE: English
AB The expression patterns of two mammalian heat shock factors (HSFs) were analysed in cell systems known to reflect an altered heat shock response. For being able to discriminate between the two closely related factors HSF 1 and HSF 2, specific cDNA sequences were cloned and used to generate **antisense** RNAs as hybridization probes. In general, in various cell lines expression of the two heat shock factors was clearly different. These expression patterns of the HSF genes were not influenced by retinoic acid-induced differentiation of human NT2 and mouse F9 teratocarcinoma cells. Generally, HSF 2 expression was extremely low, whereas the significantly higher expression of HSF 1 revealed cell specific differences. The highest expression rates of both HSFs were observed in 293 cells. To examine whether these high levels are involved in the constitutive expression of heat shock genes in these cells, we analysed the binding pattern of 293 cell proteins to the heat shock elements (**HSEs**). As with other cells, **HSE**-binding activity in 293 cells was only observed after heat shock treatment. This points to an **HSE**-independent way for high level expression of heat shock genes in these cells.

L5 ANSWER 4 OF 17 BIOSIS COPYRIGHT 2002 BIOLOGICAL ABSTRACTS INC.
ACCESSION NUMBER: 1998:28010 BIOSIS
DOCUMENT NUMBER: PREV199800028010
TITLE: Induction of heat shock protein 72 synthesis by endogenous tumor necrosis factor via enhancement of the heat shock element-binding activity of heat shock factor 1.
AUTHOR(S): Watanabe, Naoki (1); Tsuji, Naoki; Akiyama, Shinichiro; Sasaki, Hiroyoshi; Okamoto, Tetsuro; Kobayashi, Daisuke; Sato, Tsutomu; Hagino, Tsukasa; Yamauchi, Naofumi; Niitsu, Yoshiro; Nakai, Akira; Nagata, Kazuhiro
CORPORATE SOURCE: (1) Dep. Lab. Diagn., Sapporo Med. Univ., Sch. Med.,

South-1, West-16 Chuo-ku, Sapporo 060 Japan
SOURCE: European Journal of Immunology, (**Nov.**, **1997**) Vol. 27, No. 11, pp. 2830-2834.
ISSN: 0014-2980.
DOCUMENT TYPE: Article
LANGUAGE: English
AB Endogenous tumor necrosis factor (enTNF) acts as a resistance factor against cytotoxicity caused by heat by inducing manganous superoxide dismutase (MnSOD), thereby scavenging reactive oxygen free radicals. On the other hand, it is also well known that heat shock proteins (HSP) which are induced by heat stress behave as cytoprotective factor against this stress. However, the relationship of these two resistance factors is not elucidated yet. In the present study, we therefore proposed the possibility that enTNF enhances HSP72 expression. Heat-sensitive L-M (mouse tumorigenic fibroblast) cells, which normally do not express enTNF, were transfected with a nonsecretory-type human TNF-alpha expression vector to produce enTNF. Stable transfectants showed resistance to heat treatment and an increase of HSP72 expression. Conversely, when HeLa (human uterine cervical cancer) cells, which normally produce an appreciable amount of enTNF, were transfected with an **antisense** TNF-alpha mRNA expression vector to inhibit enTNF synthesis, their heat sensitivity was enhanced and HSP72 expression was reduced by half. Although enTNF caused no difference in the level of heat shock factor (HSF) 1 in these cells, enTNF expression correlated well with the binding activity of HSF-1 to a 32P-labeled synthetic oligonucleotide containing the human heat shock element (**HSE**). These results indicate that enTNF participates not only in intrinsic resistance against heat via induction of MnSOD but also via enhancement of the **HSE**-binding activity of HSF 1 followed by augmentation of HSP72 expression.

L5 ANSWER 5 OF 17 BIOSIS COPYRIGHT 2002 BIOLOGICAL ABSTRACTS INC.
ACCESSION NUMBER: 1997:409457 BIOSIS
DOCUMENT NUMBER: PREV199799701500
TITLE: Homoserine derivatives for the preparation of base-stable nucleopeptide analogues.
AUTHOR(S): Beltran, Maite; Maseda, Marta; Robles, Jordi; Pedroso, Enrique; Grandas, Anna (1)
CORPORATE SOURCE: (1) Dep. Quimica Organica, Fac. Quimica, Univ. Barcelona, Marti i Franques 1-11, E-08028 Barcelona Spain
SOURCE: Letters in Peptide Science, (1997) Vol. 4, No. 3, pp. 147-155.
ISSN: 0929-5666.
DOCUMENT TYPE: Article
LANGUAGE: English
AB Covalently linked peptide-oligonucleotide hybrids are good candidates for **antisense** or anti-gene therapeutics. The use of homoserine as the linking amino acid allows nucleopeptide analogues with a base-stable amino acid-nucleoside phosphate diester linkage to be obtained. Three N-alpha,O-protected homoserine derivatives (N-alpha-Boc-**Hse** (DMT)-O-HTEA+ (I), N-alpha-Fmoc-**Hse**(MMT)-O- Hpyr+ (II) and N-alpha-Phac-**Hse**(DMT)-O- HTEA+ (111) were prepared after transient silylation, N-alpha-acylation, desilylation and protection of the hydroxyl group. The first can be placed at any position in the peptide sequence, while the other two must be placed at the N-terminus to afford nucleopeptides with the N-terminal amine group free or permanently blocked, respectively.

L5 ANSWER 6 OF 17 BIOSIS COPYRIGHT 2002 BIOLOGICAL ABSTRACTS INC.
ACCESSION NUMBER: 1997:226070 BIOSIS
DOCUMENT NUMBER: PREV199799517786
TITLE: Heat shock and the role of the HSPs during neural plate induction in early mammalian CNS and brain development.

AUTHOR(S): Walsh, D. (1); Li, Z.; Wu, Y.; Nagata, K.
CORPORATE SOURCE: (1) Mammalian Dev. B19, Dep. Vet. Clin. Sci., Univ. Sydney, NSW 2006, Sydney Australia
SOURCE: CMLS Cellular and Molecular Life Sciences, (1997) Vol. 53, No. 2, pp. 198-211.
ISSN: 1420-682X.
DOCUMENT TYPE: General Review
LANGUAGE: English

AB We have investigated the early development expressional of the heat shock protein genes (hsps) and HSP synthesis and their role during neuroectoderm induction, differentiation and early CNS formation. The expression and kinetics of 90, 73/71, 47 and 27 HSPs on neuroectoderm differentiation was compared under normal and stressed conditions. The role of HSPs on neuroectoderm cell fate including thermotolerance and apoptosis using a whole in vitro embryo culture system was studied. Hsp expression appears closely linked in early mammalian development to critical differentiation and proliferation stages in early brain and heart formation. The hsps are developmentally activated around blastula stage and HSPs are constitutively expressed at high levels during neural tube closure and are heat shock responsive. Using both Northern analysis, confocal microscopy and whole mount in situ hybridisation we have identified the mRNA hsp transcripts and HSPs during organogenesis. HSPs were detected during neuroectoderm cell induction and differentiation with the hsp mRNA being tightly regulated during the cell cycle of neuroectoderm especially at early fore-, mid-, hindbrain and heart formation. The 'chaperone' functions of the HSPs are well known, recently during gastrulation the HSP47 and 27 have been shown to specifically bind and fold to nascent collagen and actin molecules respectively. This role is essential for the formation of the basement membrane, extra cellular matrix and neural crest migration during neural plate development. HSP function was observed by using anti-sense strategy, short '5 anti-sense cDNA' hsp **oligonucleotides inhibited** hsp expression during gastrulation in the whole embryo cultures. The developmental activation of the heat shock element (**HSE**) is essential to our understanding of the HSPs role in neuronal cell fate. Using specific polyclonal antibodies to HSF1 and 2 (Dr Nakai, Kyoto University) the expression of heat shock factors (HSFs) during neuroectoderm differentiation was examined. Using Western analysis, confocal microscopy and flow cytometry HSF1 and 2 were identified and studied under both normal and heat shocked conditions. During gastrulation higher levels of HSF1 and 2 were identified in the neuroectoderm layer especially in regions of the fore-, mid- and hindbrain. The heat shock response and activation of the HSPs 90, 70, 47 and 27 families have been correlated with HSF1 and 2. The HSF1 appears to be present in all early embryonic cells but appears not to bind to the **HSE** until early head fold stage at gastrulation when the presence of HSF2 is observed. During neuroectoderm differentiation the activation of HSF1 and 2 appears to correlate with high constitutive expression of many of the hsps specifically hsp90, 73, 71, 47 and 27 being tightly regulated by the cell cycle at neurulation.

L5 ANSWER 7 OF 17 BIOSIS COPYRIGHT 2002 BIOLOGICAL ABSTRACTS INC.
ACCESSION NUMBER: 1996:320009 BIOSIS
DOCUMENT NUMBER: PREV199699042365
TITLE: Neurotrophin stimulation of human melanoma cell invasion: Selected enhancement of **heparanase** activity and **heparanase** degradation of specific heparan sulfate subpopulations.
AUTHOR(S): Marchetti, Dario (1); McQuillan, David J.; Spohn, William C.; Carson, Dan D.; Nicolson, Garth L.
CORPORATE SOURCE: (1) Dep. Tumor Biol., Box 108, University Texas M. D. Anderson Cancer Center, 1515 Holcombe Boulevard, Houston, TX 77030 USA

SOURCE: Cancer Research, (1996) Vol. 56, No. 12, pp. 2856-2863.
ISSN: 0008-5472.

DOCUMENT TYPE: Article
LANGUAGE: English

AB **Heparanase** is an endo-beta-D-glucuronidase, the enzymatic targets of which are the glycosaminoglycan chains of heparan sulfate proteoglycans. Elevated levels of **heparanase** are associated with the metastatic potential of melanoma cells. Treatment of murine and human melanoma cells with the prototypic neurotrophin nerve growth factor (NGF) increases the production of **heparanase** by melanoma cells. We reported previously that physiological concentrations of NGF increased in vitro Matrigel invasion of early-passage human brain-metastatic 70W melanoma cells but not melanoma cells metastatic to other sites or nonmetastatic melanoma cells. Here we found that treatment of 70W melanoma cells with neurotrophin NT-3 increased Matrigel invasion, whereas treatment with neurotrophins other than NGF or NT-3 did not influence invasion. Mutants of NGF that do not bind to the neurotrophin receptor p75NTR or other nonneuronal growth factors were not able to enhance the invasion of 70W melanoma cells. When 70W cells were exposed to **antisense** oligonucleotides directed against p75-NTR mRNA, there was a reduction in NGF and NT-3 binding, and the neurotrophins failed to enhance Matrigel invasion. To study the properties of **heparanase** in NT-regulated malignant melanoma invasive processes, we developed a sensitive **heparanase** assay consisting of purified (35S)heparan sulfate subpopulations separated by agarose gel electrophoresis. Incubation of 70W cells with NGF or NT-3, but not brain-derived NT factor, NT-4/5, or mutant NGF, resulted in increased release of **heparanase** activity that was capable of degrading a subpopulation of heparan sulfate molecules.

L5 ANSWER 8 OF 17 MEDLINE
ACCESSION NUMBER: 1998132992 MEDLINE
DOCUMENT NUMBER: 98132992 PubMed ID: 9487024
TITLE: Human melanoma cell invasion: selected neurotrophin enhancement of invasion and **heparanase** activity.

AUTHOR: Marchetti D; Nicolson G L
CORPORATE SOURCE: Department of Tumor Biology, University of Texas M. D. Anderson Cancer Center, Houston 77030, USA.

CONTRACT NUMBER: R29-CA64178 (NCI)
R01-CA63045 (NCI)
SOURCE: JOURNAL OF INVESTIGATIVE DERMATOLOGY. SYMPOSIUM PROCEEDINGS, **(1997 Aug)** 2 (1) 99-105.
Journal code: 9609059. ISSN: 1087-0024.

PUB. COUNTRY: United States
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 199803
ENTRY DATE: Entered STN: 19980319
Last Updated on STN: 19980319
Entered Medline: 19980310

AB **Heparanase** is an endo-beta-D-glucuronidase whose enzymatic targets are the glycosaminoglycan chains of heparan sulfate proteoglycans. Elevated levels of **heparanase** are associated with the metastatic potential of melanoma cells. Treatment of murine and human melanoma cells with the prototypic neurotrophin nerve growth factor (NGF) increases the production of **heparanase** by melanoma cells. We previously reported that physiologic concentrations of NGF increased in vitro Matrigel invasion of early passage human brain-metastatic 70W melanoma cells but not melanoma cells metastatic to other sites or nonmetastatic melanoma cells. Here we found that treatment of 70W melanoma cells with neurotrophin-3 (NT-3) increased Matrigel invasion, whereas treatment with

neurotrophins other than NGF or NT-3 did not influence invasion. Mutants of NGF that do not bind to the neurotrophin receptor p75NTR or other nonneuronal growth factors were not able to enhance the invasion of 70W melanoma cells. When 70W cells were exposed to anti-sense oligonucleotides directed against p75NTR mRNA, there was a reduction in NGF and NT-3 binding, and the neurotrophins failed to enhance Matrigel invasion. To study to properties of **heparanase** in NT-regulated melanoma-invasive processes, we developed a sensitive **heparanase** assay consisting of purified [35S]heparan sulfate subpopulations separated by agarose gel electrophoresis. Incubation of 70W cells with NGF or NT-3, but not BDNF, NT-4/5, or mutant NGF, resulted in increased release of **heparanase** activity that was capable of degrading a subpopulation of heparan sulfate molecules.

L5 ANSWER 9 OF 17 MEDLINE
ACCESSION NUMBER: 1998020941 MEDLINE
DOCUMENT NUMBER: 98020941 PubMed ID: 9381967
TITLE: Neurotrophin stimulation of human melanoma cell invasion: selected enhancement of **heparanase** activity and **heparanase** degradation of specific heparan sulfate subpopulations.
AUTHOR: Marchetti D; Nicolson G L
CORPORATE SOURCE: Department of Tumor Biology, University of Texas M. D. Anderson Cancer Center, Houston 77030, USA.
CONTRACT NUMBER: R29-CA64178 (NCI)
R01-CA44352 (NCI)
SOURCE: ADVANCES IN ENZYME REGULATION, **(1997)** 37 111-34.
Journal code: 0044263. ISSN: 0065-2571.
PUB. COUNTRY: ENGLAND: United Kingdom
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 199711
ENTRY DATE: Entered STN: 19971224
Last Updated on STN: 20000303
Entered Medline: 19971110

AB **Heparanase** is an endo-beta-D-glucuronidase whose enzymatic targets are the glycosaminoglycan chains of heparan sulfate proteoglycans (50). Elevated levels of **heparanase** are associated with the metastatic potential of melanoma cells, and treatment of murine and human melanoma cells with the prototypic neurotrophin nerve growth factor (NGF) increases the production of **heparanase** by melanoma cells. We previously reported that physiological concentrations of NGF increased invasion of early passage human brain-metastatic 70W melanoma cells but not melanoma cells metastatic to other sites or nonmetastatic melanoma cells as measured in Matrigel invasion assays. Here we found that treatment of 70W melanoma cells with neurotrophin-3 (NT-3) increased Matrigel invasion, whereas treatment with neurotrophins other than NGF or NT-3 did not influence invasion. Mutants of NGF that do not bind to the neurotrophin receptor p75NTR or other nonneuronal growth factors were not able to enhance the invasion of 70W melanoma cells. When 70W cells were exposed to **antisense** oligonucleotides directed against p75NTR mRNA, there was a reduction in NGF and NT-3 binding, and the neurotrophins failed to enhance Matrigel invasion. To study the properties of **heparanase** in neurotrophin-regulated malignant melanoma invasive processes, we developed a sensitive **heparanase** assay consisting of purified [35S]HS subpopulations separated by agarose gel electrophoresis. Incubation of 70W cells with NGF or NT-3 but not brain-derived neurotrophic factor, neurotrophin-4/5 or mutant NGF resulted in increased release of **heparanase** activity that was capable of degrading a subpopulation of heparan sulfate molecules.

L5 ANSWER 10 OF 17 SCISEARCH COPYRIGHT 2002 ISI (R)
ACCESSION NUMBER: 1999:203054 SCISEARCH
THE GENUINE ARTICLE: 173TW
TITLE: The Hsp70 homolog gene, Hsc70t, is expressed under translational control during mouse spermiogenesis
AUTHOR: Tsunekawa N; Matsumoto M; Tone S; Nishida T; Fujimoto H (Reprint)
CORPORATE SOURCE: MITSUBISHI KASEI INST LIFE SCI, 11 MINAMIOOYA, MACHIDA, TOKYO 1948511, JAPAN (Reprint); MITSUBISHI KASEI INST LIFE SCI, MACHIDA, TOKYO 1948511, JAPAN; NIHON UNIV, COLL BIORESOURCE SCI, LAB ANAT & PHYSIOL, KANAGAWA, JAPAN
COUNTRY OF AUTHOR: JAPAN
SOURCE: MOLECULAR REPRODUCTION AND DEVELOPMENT, **(APR 1999***)** **Vol. 52, No. 4, pp. 383-391.**
Publisher: WILEY-LISS, DIV JOHN WILEY & SONS INC, 605 THIRD AVE, NEW YORK, NY 10158-0012.
ISSN: 1040-452X.
DOCUMENT TYPE: **Article; Journal**
FILE SEGMENT: **LIFE**
LANGUAGE: **English**
REFERENCE COUNT: 56

ABSTRACT IS AVAILABLE IN THE ALL AND IALL FORMATS

AB **Hsc70t is a member of the Hsp70 family of genes and is constitutively expressed after meiosis in mouse spermatogenesis. Immunohistochemistry and in situ hybridization techniques were used to examine the precise localization of the Hsc70t product during the various stages of spermatogenesis. A rabbit antiserum raised against the mouse ***Hse** 70t-lacZ fusion protein detected the Hsc70t protein in the late spermatid-enriched fraction after two-dimensional Western blot analyses. On histological sections, the protein appears in the cytoplasm of spermatids as they progress from step 9 to the final step of spermatogenesis. An **antisense** RNA probe generated from the 3' untranslated region of **Hse** 70t cDNA detected **Hse** 70t mRNA in late round spermatids from step 7 onward with the signal disappearing in spermatids at step 15. Thus, Hsc70t mRNA first appears after meiosis in haploid cells but is not translated effectively until these cells progress to the transcriptionally inactive stage which coincides with chromatin condensation. These results establish that the synthesis of Hsc70t protein is under strict translational control. (C) 1999 Wiley-Liss, Inc.

L5 ANSWER 11 OF 17 SCISEARCH COPYRIGHT 2002 ISI (R)
ACCESSION NUMBER: 96:697280 SCISEARCH
THE GENUINE ARTICLE: VH657
TITLE: AN HSP70 **ANTISENSE** GENE AFFECTS THE EXPRESSION OF HSP70/HSC70, THE REGULATION OF HSF, AND THE ACQUISITION OF THERMOTOLERANCE IN TRANSGENIC ARABIDOPSIS-THALIANA
AUTHOR: LEE J H; SCHOFFL F (Reprint)
CORPORATE SOURCE: UNIV TUBINGEN, LEHRSTUHL ALLGEMEINE GENET, MORGENSTELLE 28, D-72076 TUBINGEN, GERMANY (Reprint); UNIV TUBINGEN, LEHRSTUHL ALLGEMEINE GENET, D-72076 TUBINGEN, GERMANY
COUNTRY OF AUTHOR: GERMANY
SOURCE: MOLECULAR & GENERAL GENETICS, **(27 AUG 1996)** Vol. 252, No. 1-2, pp. 11-19.
ISSN: 0026-8925.
DOCUMENT TYPE: Article; Journal
FILE SEGMENT: LIFE
LANGUAGE: ENGLISH
REFERENCE COUNT: 49

ABSTRACT IS AVAILABLE IN THE ALL AND IALL FORMATS

AB The genes and proteins of the HSP70 family, are involved in important processes in cells and organelles at normal temperature and after heat

stress. Constitutive **Hse** 70 and heat-inducible Hsp 70 genes are known in all organisms including plants. The goal of our present investigation was to generate an Hsp70 mutation in Arabidopsis thaliana. In a transgenic approach a heat-inducible **antisense** Hsp70 gene was constructed, plants were transformed and screened for lack of heat-inducible HSP70 mRNA; two such lines were further investigated. In these plants the Hsp 70 gene was not induced by heat shock, and the level of HSC70 RNA was also greatly reduced. This negative **antisense** effect was specific for genes of the HSP70 family and the induction of mRNAs encoding the small HSP18 class of heat shock protein (HSP) was not affected. The level of HSP70/HSC70 proteins was significantly reduced in transgenic plants, but HSP18 was induced to the same level in different transgenic lines and in untransformed plants. The acquisition of thermotolerance was negatively affected in artisense plants, the survival temperature being 2 degrees C below the survival temperature of the wild type and other transgenic lines. Another major effect concerning the regulation of the endogenous heat shock transcription factor HSF was detected by testing the ability to form heterotrimers between authentic HSF and recombinant HSF-GUS (beta-glucuronidase) proteins. The shut-off time, required to turn off HSF activity during recovery from heat stress, was significantly prolonged in **antisense** plants compared with wild-type and other transgenic lines. Our results imply a dual role of HSP70 in plants, a protective role in thermotolerance and a regulatory effect on HSF activity and hence the autoregulation of the heat shock response.

L5 ANSWER 12 OF 17 CA COPYRIGHT 2002 ACS
ACCESSION NUMBER: 133:219460 CA
TITLE: A **heparanase** playing a role in cancer and cloning and expression of the gene encoding it and its therapeutic uses
INVENTOR(S): Pecker, Iris; Vlodavsky, Israel; Feinstein, Elena
PATENT ASSIGNEE(S): Insight Strategy and Marketing Ltd., Israel; Hadasit Medical Research Services and Development Ltd.; Friedman, Mark, M.
SOURCE: PCT Int. Appl., 152 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 15
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2000052178	A1	20000908	WO 2000-US3542	20000214 <--
W: AE, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CR, CU, CZ, DE, DK, DM, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, GM, KE, LS, MW, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
EP 1157118	A1	20011128	EP 2000-907262	20000214
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO				

PRIORITY APPLN. INFO.: US 1999-258892 A 19990301
WO 2000-US3542 W 20000214

AB A **heparanase** that may be involved in neoplastic processes is identified and characterized and a cDNA encoding it is cloned. **Antisense** oligonucleotides and constructs for modulating

heparanase expression are described. ESTs encoding the enzyme were identified using amino acid sequence-derived sequences to query public databases. ESTs were converted to full-length cDNAs by RACE. Enzyme manufd. by expression of the clones in Escherichia coli was able to remove heparan sulfate from heparan sulfate proteoglycans.

REFERENCE COUNT: 4 THERE ARE 4 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L5 ANSWER 13 OF 17 CA COPYRIGHT 2002 ACS
ACCESSION NUMBER: 131:350261 CA
TITLE: **Heparanase** specific molecular probes and their use in research and medical applications
INVENTOR(S): Pecker, Iris; Vlodavsky, Israel; Friedman, Yael; Perets, Tuvia
PATENT ASSIGNEE(S): Insight Strategy & Marketing Ltd., Israel; Hadasit Medical Research Services & Development Ltd.; Friedman, Mark, M.
SOURCE: PCT Int. Appl., 90 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 15
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE	
WO 9957153	A1	19991111	WO 1999-US9255	19990429	<--
W: AE, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM					
RW: GH, GM, KE, LS, MW, SD, SL, SZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG					
US 6177545	B1	20010123	US 1998-71739	19980501	
AU 9938706	A1	19991123	AU 1999-38706	19990429	<--
EP 1073682	A1	20010207	EP 1999-921513	19990429	
R: AT, BE, CH, DE, DK, ES, FR, GB, IT, LI, NL, SE, IE, FI					
JP 2002512533	T2	20020423	JP 1999-555528	19990429	
NO 9906229	A	20000224	NO 1999-6229	19991215	<--

PRIORITY APPLN. INFO.:
US 1998-71739 A 19980501
US 1997-922170 A2 19970902
WO 1999-US9255 W 19990429

AB A variety of **heparanase** specific mol. probes which can be used for research and medical applications including diagnosis and therapy. Specific applications include the use of a **heparanase** specific mol. probe for detection of the presence, absence or level of **heparanase** expression; the use of a **heparanase** specific mol. probe for therapy of a condition assocd. with expression of **heparanase**; the use of a **heparanase** specific mol. probe for quantification of **heparanase** in a body fluid; the use of a **heparanase** specific mol. probe for targeted drug delivery; and the use of a **heparanase** specific mol. probe as a therapeutic agent.

REFERENCE COUNT: 14 THERE ARE 14 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L5 ANSWER 14 OF 17 CA COPYRIGHT 2002 ACS
ACCESSION NUMBER: 130:218305 CA
TITLE: **Antisense** inhibition of endothelin-1 gene expression in treatment of pulmonary hypertension

INVENTOR(S): Higenbottam, Timothy; McCormack, Keith; Smith, Adrian
PATENT ASSIGNEE(S): University of Sheffield, UK
SOURCE: PCT Int. Appl., 35 pp.
CODEN: PIXXD2

DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9911778	A1	19990311	WO 1998-GB2584	19980902 <--
W: AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GE, GH, GM, HR, HU, ID, IL, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, US, UZ, VN, YU, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, GM, KE, LS, MW, SD, SZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
CA 2302167	AA	19990311	CA 1998-2302167	19980902 <--
AU 9888741	A1	19990322	AU 1998-88741	19980902 <--
EP 1009822	A1	20000621	EP 1998-940410	19980902 <--
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, NL, SE, PT, IE, FI				
JP 2001515011	T2	20010918	JP 2000-508789	19980902
			GB 1997-18487 A	19970902
			WO 1998-GB2584 W	19980902

PRIORITY APPLN. INFO.:

AB The invention herein described relates to a method to treat pulmonary hypertension by **antisense** therapy using ET-1 derived **antisense** mols. delivered to the lungs as a pulse/spike in an inhaler. **Antisense** oligonucleotides are designed complementary to the promoter region and the intron-exon splice junctions of both human and rat endothelin-1 (ET-1) genes.

REFERENCE COUNT: 7 THERE ARE 7 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L5 ANSWER 15 OF 17 CA COPYRIGHT 2002 ACS
ACCESSION NUMBER: 130:76154 CA
TITLE: P53 as a regulator of cell differentiation, and method of screening for differentiation agents

INVENTOR(S): Vize, Peter D.; Wallingford, John B.
PATENT ASSIGNEE(S): Board of Regents, the University of Texas System, USA
SOURCE: PCT Int. Appl., 71 pp.
CODEN: PIXXD2

DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9901763	A2	19990114	WO 1998-US13797	19980701 <--
WO 9901763	A3	19990325		
W: AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GE, GH, GM, GW, HU, ID, IL, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, US, UZ, VN, YU, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, GM, KE, LS, MW, SD, SZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG				
AU 9882841	A1	19990125	AU 1998-82841	19980701 <--

ZA 9805833 A 19990114 ZA 1998-5833 19980702 <--
PRIORITY APPLN. INFO.: US 1997-51549P P 19970702
US 1997-515494P P 19970701
WO 1998-US13797 W 19980701

AB The invention involves the role of p53 in the differentiation of embryonic tissues. More particularly, the invention provides methods of the blocking of p53 function in embryonic tissues, and the use of these tissues as screening tools for substances that are capable of overcoming the p53-related block in differentiation, both in vitro and in vivo. The similarities between undifferentiated embryonic cells and tumor cells is evident, and thus these assays serve as a model for possible cancer therapeutics. In addn., methods for identifying addnl. cellular components that interact p53 or p53-related pathways are provided.

L5 ANSWER 16 OF 17 CA COPYRIGHT 2002 ACS
ACCESSION NUMBER: 129:50527 CA
TITLE: Cloning and sequence of human selenium-binding protein **HSEBP** gene
INVENTOR(S): Bandman, Olga; Hawkins, Phillip R.
PATENT ASSIGNEE(S): Incyte Pharmaceuticals, Inc., USA
SOURCE: U.S., 35 pp.
CODEN: USXXAM
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 5759812	A	19980602	US 1996-749903	19961115 <--
US 6312895	B1	20011106	US 1998-88641	19980602
US 2002042066	A1	20020411	US 2001-841758	20010424

PRIORITY APPLN. INFO.: US 1996-749903 A3 19961115
US 1998-88641 A3 19980602

AB The present invention provides a human selenium-binding protein (**HSEBP**) and polynucleotides which identify and encode **HSEBP** . The invention also provides genetically engineered expression vectors and host cells comprising the nucleic acid sequences encoding **HSEBP** and a method for producing **HSEBP**. The invention also provides for agonists and antibodies specifically binding **HSEBP**, and their use in the prevention and treatment of diseases assocd. with expression of **HSEBP**. Addnl., the invention provides for the use of **antisense** mols. to polynucleotides encoding **HSEBP** for the treatment of diseases assocd. with the expression of **HSEBP**. The invention also provides diagnostic assays which utilize the polynucleotide, or fragments or the complement thereof, and antibodies specifically binding **HSEBP**.

L5 ANSWER 17 OF 17 CA COPYRIGHT 2002 ACS
ACCESSION NUMBER: 125:105151 CA
TITLE: Glycosaminoglycan-degrading enzyme inhibition with phosphorothioate- or phosphorodithioate-containing oligonucleotides and resultant disease therapies
INVENTOR(S): Graham, Lloyd; Underwood, Patricia Anne
PATENT ASSIGNEE(S): Cardiac Crc Nominees Pty. Ltd., Australia
SOURCE: PCT Int. Appl., 72 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9608559	A1	19960321	WO 1995-AU600	19950913 <--
W: AU, JP, US RW: AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE				
AU 9535145	A1	19960329	AU 1995-35145	19950913 <--

PRIORITY APPLN. INFO.:

AU 1994-8226	19940916
AU 1994-8227	19940916
AU 1995-4769	19950814
WO 1995-AU600	19950913

AB Methods for the inhibition of glycosaminoglycan-degrading enzymes are described. These methods involve reacting glycosaminoglycan-degrading enzymes or cells producing the same with an oligonucleotide characterized in that at least one backbone linkage between adjacent nucleosides in the oligonucleotide is substituted with one or more sulfur atoms. Also described are methods for the treatment of disease assocd. with glycosaminoglycan-degrading enzymes. Nine different phosphorothioate-linked oligonucleotides were prepd. and tested as inhibitors of bacterial heparinases and mammalian **heparanases**. Length, base compn., and no. of S atoms were determinants of inhibitory activity. The phosphorothioate-linked **oligonucleotides inhibited** activation and proliferation of rabbit vascular smooth muscle cells.

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(FILE 'HOME' ENTERED AT 09:44:50 ON 20 AUG 2002)

FILE 'BIOSIS, MEDLINE, SCISEARCH, CA' ENTERED AT 09:45:01 ON 20 AUG 2002

L1	5707	S HEPARANASE? OR HSE?
L2	78393	S ANTISENSE OR (OLIGONUCL? (2N) INHIB?)
L3	46	S L1 AND L2
L4	24	DUP REM L3 (22 DUPLICATES REMOVED)
L5	17	S L4 AND PY=<2000